UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/971,894 | 10/09/2001 | Yechezkel Kashi | 01/22569 | 3442 |

7590 12/29/2003

G E EHRLICH
C/O ANTHONY CASTORINA
2001 JEFFERSON DAVIS HIGHWAY
SUITE 207
ARLINTON, VA 22202

| EXAMINER | |
|---|---|
| FREDMAN, JEFFREY NORMAN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/971,894 | KASHI ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 November 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16,17,19,20,23-30,33-35,37,38,41-44,46,47,50 and 51* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17,25-28,35,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continuation of Disposition of Claims: Claims withdrawn from consideration are 19,20,23,24,29,30,33,34,37,38,41,42,46,47,50 and 51.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16-17, 25-28, 35, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are defined solely by function, without any structural elements whatsoever. These nucleic acids are not disclosed in the specification. Specifically, claim 16, for example, is drawn to any primers which function to amplify any generic sequence which has simple sequence

repeats. This genus, which is literally comprises many hundreds of trillions of differerent possible sequences, is represented in the specification by only the particularly named SEQ ID Nos. Thus, applicant has express possession of, at most, 42 different sequences which amplify such repeats, in a genus which comprises hundreds of trillions of different possibilities. Here, no common element or attributes of the sequences are disclosed. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the primers, probes and gene chips is precisely the situation of naming a type of material which is generally known to likely exist, but, except for those disclosed, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to any "sequence-adapted

for exponential amplification of a polymorphic simple sequence repeat locus in a genome of a prokaryote", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a primer or probe, without any definition of the particular sequence, the particular chemical structure of the primers which amplify the SSR sequences, or any particular element that is common to primers which amplify SSR sequences.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 16, 17, 25-28 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Rasmussen et al (Microbiology (1995) 141:2053-2061).

Rasmussen teaches a series of PCR primers and probes which amplify SSR regions in Listeria monocytogenes (see page 2054, column 2). In particular, the primers which amplify the 23S gene, which is a non-coding gene since it does not encode any protein sequence, meet the requirements of the claim. (see page 2057). On page 2056, various accession numbers of the 23S gene are provided, including X85897, reproduced below:

```
LOCUS       LM23SGT31               233 bp    DNA     linear   BCT 08-MAR-2000
DEFINITION  L.monocytogenes partial 23S rRNA gene (strain T31).
ACCESSION   X85897
VERSION     X85897.1  GI:940575
KEYWORDS    23S ribosomal RNA; 23S rRNA gene.
SOURCE      Listeria monocytogenes
  ORGANISM  Listeria monocytogenes
            Bacteria; Firmicutes; Bacillales; Listeriaceae; Listeria.
REFERENCE   1  (bases 1 to 233)
  AUTHORS   Rasmussen,O.F., Skouboe,P., Dons,L., Rossen,L. and Olsen,J.E.
  TITLE     Listeria monocytogenes exists in at least three evolutionary lines:
            evidence from flagellin, invasive associated protein and
            listeriolysin O genes
  JOURNAL   Microbiology (Reading, Engl.) 141 (Pt 9), 2053-2061 (1995)
  MEDLINE   96118685
   PUBMED   7496516
REFERENCE   2  (bases 1 to 233)
  AUTHORS   Skouboe,P.
  TITLE     Direct Submission
  JOURNAL   Submitted (27-MAR-1995) P. Skouboe, Biotechnological Institute,
            Anker Engelunds Vej 1, Building 227, DK-2800 Lyngby, DENMARK
COMMENT     Related sequence
            X64533 Thompson et al, FEMS Microbiol. Lett., 96, 219-224, 1992.
FEATURES             Location/Qualifiers
     source          1..233
                     /organism="Listeria monocytogenes"
                     /mol_type="genomic DNA"
                     /strain="T31"
                     /db_xref="taxon:1639"
                     /note="Part of the 23S rRNA gene. 1350-1580, numbers
```

```
                     according to X64533"
     gene            1..233
                     /gene="23S rRNA"
     rRNA            <1..>233
                     /gene="23S rRNA"
                     /product="23S ribosomal RNA"
     variation       63..64
                     /gene="23S rRNA"
                     /note="insertion in strain T31, equivalent position
                     1411^1412 in X64533"
                     /replace="gg"
ORIGIN
        1 taaggtttcc tgaggaaggc tcgtccgctc agggttagtc gggacctaag ccgaggccga
       61 taggcgtagg cgatggacaa caggtagaga ttcctgtacc agtgctaatt gtttaaccga
      121 tggggtgaca cagaaggata gggaatcgca cgaatggaaa tgtgcgtcca agcagtgagt
      181 gtgagaagta ggcaaatccg cttctcgcga agcatgagct gtgatgggga agg
```

A review of the sequence demonstrates the presence of several simple sequence repeats of more than four nucleotides, including GGGG at positions 122-125.

### *Claim Rejections - 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rasmussen et al (Microbiology (1995) 141:2053-2061) as applied to claims 16, 17, 25-28 and 35 above and further in view of Gingeras (U.S. Patent 6,228,575).

Rasmussen teaches the limitations of claims 16, 17, 25-28 and 35 as discussed above.

Rasmussen does not teach diagnosis of Listeria monocytogenes using DNA chips.

Gingeras teaches a method of detecting Listeria by detecting nucleic acids on a DNA chip (see claims 1 and 78 and columns 7 and 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the DNA chip of Gingeras in the detection method of Rasmussen since Gingeras states "This invention provides methods, compositions and devices for identifying the group or species of an organism and obtaining functional phenotypic information about the organism based on genotypic analysis of one or more genomic regions of the organism (see column 7, lines 50-54)." An ordinary practitioner would have been motivated to use the probes and primers of Rasmussen in the Gene chip of Gingeras in order to identify the various types of Listeria monocytogenes as expressly motivated by both Rasmussen and Gingeras. The motivation to use a gene chip would arise because Gingeras teaches that this is a simple method to identify and characterize organisms (see column 2, lines 60-62).

***Response to Arguments***

8. Applicant's arguments filed November 12, 2003 have been fully considered but they are not persuasive.

Applicant argues that there is support for the structure of the claims. However, a particularly apropos part of the Federal Circuit decision in Enzo notes that the function of the nucleic acid must be correlated to a "structure that is sufficiently known or disclosed". However, in the current case, there is no function whatsoever and there is no function that is correlated or tied to any structure, because no primer sequence is required. That is, not only are the claims open to any pair of primers selected from the entire Listeria genome, but the claims are open to any random set of primers which will, as in methods such as differential display, function to amplify the Listeria genome. Thus, any primer pair whatsoever reads on these claims.

Applicant attempts to distinguish genes from primers, and rely upon published sequence information. However, applicant provides no structure for these primers whatsoever. For example, random hexamers are frequently used for such amplifications. Therefore, the function of amplifying the repeats identified by Applicant is not sufficient to distinguish the primer requirements in any meaningful way.

Applicant argues that there is sufficient description of species in the claimed genus to overcome the written description rejection. Applicant details that they have identified many such simple sequence repeats. However, Applicant is not claiming the repeats. Applicant is not claiming a method of detecting the repeats. Applicant is claiming any primers which function to amplify the repeats, without providing any sequence information or any structural information for these primers. When Applicant

relies upon the genus species analysis of the written description guidelines, this analysis is based upon the assumption that there will be insubstantial variation, as noted in many of the examples including example 10. However, Applicant's analysis is flawed since there is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the nucleic acid to hybridize. However, hybridization is an inherent capability of nucleic acids, and amplification, in particular, can be achieved with non specific primers. Many methods, ranging from ARMS to differential display, specifically rely on the fact that nonspecific unrelated nucleic acids are capable of amplifying specific targets. So the argument by Applicant that there would be insubstantial variation is not correct since the function of hybridizing and amplifying does not limit the nucleic acid in any significant way. As noted previously, random hexamers would be capable of meeting the claim limitation of amplifying the target nucleic acid.

Applicant appears to also be making the argument that the size of the genus is not relevant. This is not found persuasive because the size of the genus is a central issue. If the genus were small, a written description rejection would be less likely, since the examples would be more representative of the genus. Here, where the genus includes nearly every possible nucleic acid primer, literally trillions and trillions of possible molecules, none of which are disclosed or taught by Applicant, the argument that the demonstrated species is representative is not found persuasive.

Applicant argues the prior art rejections of Rasmussen differs from the invention in that the repeats are not in hypervariable regions. No such requirement is in the

claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the polymorphic site is not in a noncoding region. Rasmussen also teaches sequencing from the 23S gene, which is clearly non coding sequence (see page 2057). This change in Rasmussen was necessitated by Applicant's amendment. Applicant's remaining arguments are consequently moot.

***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634